UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/922,226	08/02/2001	Yi Zhao	17432 (HL)	8912

23601 7590 02/24/2004

CAMPBELL & FLORES LLP
4370 LA JOLLA VILLAGE DRIVE
7TH FLOOR
SAN DIEGO, CA 92122

EXAMINER	
BASI, NIRMAL SINGH	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 02/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/922,226	ZHAO ET AL.	
	Examiner	Art Unit	
	Nirmal S. Basi	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *16 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-68* is/are pending in the application.

4a) Of the above claim(s) *35-68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *09 January 2002 and 16 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group I (Claims 1-34) and election of species RXR on 11/16/03, is acknowledged. The traversal is on the ground(s) that it would not be a serious burden to examine the groups together. This is not found persuasive because a search of groups I-III would not be co-extensive particularly with regard to the literature search. An examination of the materially different, patentably distinct inventions in a single application would constitute a serious undue burden on the examiner.

The requirement is still deemed proper and is therefore made FINAL.

Objections

2. The description of the drawings objected to because each Figure must described separately in the Brief Description of the Drawings and the first descriptor of the Figures show all the subsets, i.e. Figure 1 must be labeled as Figures 1A-C, and described separately as Figure 1A, 1B and 1C or the equivalent, as required by 37 C.F.R. § 1.84 (u)(1). Figures 3, 5, 611, 12, 13, 14, 17, and 18 must also be described in the Brief Description of the Drawings as disclosed above.

Appropriate correction is required.

3. ***Sequence Rules Compliance***

This application fails to comply with the sequence rules, 37 CFR 1.821-1.825. Nucleotide and polypeptide sequences must be identified with the corresponding

SEQ ID NO. Title 37, Code of Federal Regulations, Section 1.821 states "reference must be made to the sequence by use of the assigned identifier", the identifier being SEQ ID NO. Sequences on pages 8 and 33 must be identified by their corresponding SEQ ID NO:. Correction is required throughout the specification. Compliance with sequence rules is required.

4. The proposed drawing correction and/or the proposed substitute sheets of drawings (Figures 2), filed on 1/9/02 has been approved by the Examiner.

Claim Rejection, 35 U.S.C. 112

5. Claims 1-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, 11, 14 are indefinite because it is not clear what is an altered modification state, specifically what is modified, and further, what biological activity is modulated by the altered modification state, so as to allow the metes and bounds of the claim to be determined. Also it is not clear what conditions are considered suitable for modification. Since the modification state and biological activity are not disclosed it is not clear what conditions would be considered suitable for modification. Also it is not clear which part of the nuclear hormone receptor and agent complex is modified so as to modulate a biological activity. Further, it is unclear what is a control modification state, what is modified. What is compared to determine if an altered modification state has occurred?

Claim 2 is indefinite because it is not clear what biological activity is modulated by the altered modification state, so as to allow the metes and bounds of the claim to be determined. Also it is not clear which part of the nuclear hormone receptor and agent complex is modified (phosphorylated) so as to modulate a biological activity. Further, it is unclear what is a control phosporylation state. Is the control phosporylation state the phospohorylation state of the complex before applying conditions suitable for phosphorylation, is it the phosphorylation state of the nuclear hormone receptor and agent prior to modification, etc.

Claim 5 is indefinite because it is not clear what biological activity is modulated by the altered modification state, so as to allow the metes and bounds of the claim to be determined. Further, it is unclear what is a control phosporylation state. Is the control phosporylation state the phospohorylation state of the complex before applying conditions suitable for phosphorylation, is it the phosphorylation state of the nuclear hormone receptor and agent prior to modification, etc. Further the name 160 kDa protein doe not provide sufficient structural and functional information about the protein so as to allow the metes bounds of the claim to be determined. Also it must be noted that the calculated molecular weight of a protein depends upon the method used for said determination. The method used for determining molecular weight has not been disclosed.

Claim 7 is indefinite because the name 160 kDa protein doe not provide sufficient structural and functional information about the protein so as to allow the metes bounds of the claim to be determined. Also it must be noted that the calculated molecular

weight of a protein depends upon the method used for said determination. The method used for determining molecular weight has not been disclosed.

Claim 17 is indefinite because it is not clear what is considered the native DNA-binding domain so as to allow the metes and bounds of the claim to be determined. More specifically when is a domain considered native as compared to not native, and further native to what?

The term "consists essentially of" renders the claim 18 indefinite because it is not clear when the truncated nuclear hormone receptor consists essentially of the ligand-binding domain as compared to when it does not consist essentially of the ligand-binding domain.

Claim 19 is indefinite because the term "variant" provides no information about the structure of the nuclear hormone receptor since no nuclear hormone receptor is disclosed. Further it is not clear what is considered the wild type nuclear hormone receptor so as to allow the metes and bounds of the claim to be determined.

Claim 20 is indefinite because the term "variant" provides no information about the structure of the nuclear hormone receptor since no nuclear hormone receptor is disclosed. Further it is not clear what is considered the functional DNA binding so as to allow the metes and bounds of the claim to be determined

Claim 21 is indefinite because it is not clear what structure comprises the membrane-anchoring domain since no specific nuclear hormone receptor is disclosed in the claim.

Claim 23 is indefinite because it is not clear what structure comprises the protein kinase recognition sequence since no specific nuclear hormone receptor is disclosed in the claim.

Claim 24 is indefinite because it is not clear what constituents comprise the specific binding agents in step (b).

Claim 29 is indefinite because it is not clear what structure comprises the exogenous heterodimeric partner since no specific nuclear hormone receptor is disclosed in the claim. Further, all nuclear hormone receptors may not have an exogenous heterodimeric partner.

Claim 30 is indefinite because it is not clear what is the altered modification state.

Claims 3, 4, 6, 8-11, 12-13, 15-16, 22, 25-28 and 31-34 are rejected for depending upon indefinite base (or intermediate) claim and fail to resolve the issues raised above.

Claim Rejection, 35 U.S.C. 112

6. Claims 1-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying an effective agent that modulates phosphorylation of retinoid X receptor, wherein the retinoid X receptor comprises RXRα or truncated retinoid X receptor comprising residues 259-463 of SEQ ID NO:1, comprising the steps of (a) contacting said nuclear hormone receptor with one or more agents and a eukaryotic cell sample to form a test sample under conditions suitable to form a receptor-containing complex; (b) isolating said receptor-containing

complex from said test sample; (c) providing to said isolated receptor-containing complex specific conditions suitable for phosphorylation of said receptor-containing complex; and (d) assaying said isolated receptor-containing complex for an altered phosphorylation state occurring in said receptor-containing complex as compared to a control state (control state being step (c) lacking conditions suitable for phosphorylation), wherein the presence of said altered phosphorylation state indicates that at least one agent of said one or more agents is an effective agent that modulates phosphorylation of the retinoid X receptor, does not reasonably provide enablement for other nuclear hormone receptors or other altered modification states. The, specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification discloses that in the presence of RXR-specific ligand (AGN194204), nuclear retinoid X receptor (RXRα) and the truncated retinoid X receptor comprising residues 259-463 of SEQ ID NO:1, immunoprecipitate at least one kinase that phosphorylates RXR and another protein with a molecular weight of 160kDa. The RXR lignad binding is concluded to enhance recruitment of a kinase to RXR. Both RXR and the 160 kDa protein were phosphorylated on both serine and threonine residues but not on tyrosine. The specification discloses only the phosphoryaltion associated with immunoprecipitation of RXRα or truncated RXRα when assayed as disclosed above.

While the person of ordinary skill in the art would, in light of the specification be able to isolate and assay the retinoid X receptor comprising RXRα or truncated retinoid X receptor comprising residues 259-463 of SEQ ID NO:1, in an assay to determine an altered modification sate (phosphorylation) , the scope of the claims, which encompass other receptors and other biological activities are not enabled by the disclosure. All receptors are not capable of maintaining the receptor-congaing complex of the test sample (step (b) of the claims, and may not be capable of being modified as claimed in step (c), The disclosure does not teach how to make and use all the nuclear hormone receptors encompassed by the claims, retaining an altered biological state that indicates that at least one or more agents are effective at modulating biological activity of the nuclear hormone receptor. Further only one truncated form of the RXR has been disclosed to be phosphorylated by claimed method. The nature of the 160 kDa protein is not disclosed. Claim 1 does not disclose the specific activity that is associated with the biological function. The variants that lack functional DNA binding domains, except truncated retinoid X receptor comprising residues 259-463 of SEQ ID NO:1, that would be assayable by claimed method are not disclosed. Further the claims do not disclose the specific conditions suitable for modification of other receptor containing complexes, except for RXR. Since receptors have different functions, different ligands and different modification states said conditions are critical to isolation of functional receptor-agent complex. Further the disclosure does not disclose the structural limitations required to produce truncated polypeptides, variants and the 160kDa protein described above , which retain biological activity . Instant specification does not teach which particular

amino acids are critical for the production of the receptor-containing complex, the dimer partner, since orphan receptors are also contemplated by the invention. Therefore, the lack of guidance provided in the specification as to what other nuclear hormone receptors may be isolated in a receptor-contain complex and be modified to give an altered modification state indicative of a modulated biological activity would require undue experimentation of the skilled artisan to make or use the claimed invention in its full scope.

7. A copy of the considered IDS will be provided in the next Office Action. During the course of scanning the application in to the eDAN system the legibility of the IDS was compromised. The IDS is being rescanned.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal S. Basi whose telephone number is 571-272-0868. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nirmal Basi NJB
Art Unit 1646
2/22/04

Michael D. Pak
MICHAEL PAK
PRIMARY EXAMINER